EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L3	1072	514/247.ccls. 514/252.01.ccls. 514/252.02.ccls. 514/252.03.ccls. 514/252.04.ccls. 514/252.05.ccls. 514/252.06.ccls.	US-PGPUB; USOCR	OR	ON	2007/09/10 12:16
L4	1655	514/247.ccls. 514/252.01.ccls. 514/252.02.ccls. 514/252.03.ccls. 514/252.04.ccls. 514/252.05.ccls. 514/252.06.ccls.	USPAT	OR	ON	2007/09/10 12:16

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L9                STR
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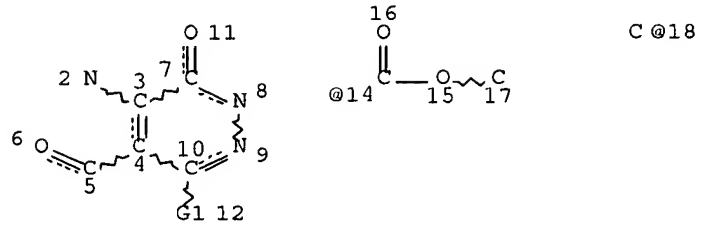

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L14           37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L16           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND(1840-2003)/PRY,AY,
                 PY


=> s l16 not l25
L42           5 L16 NOT L25

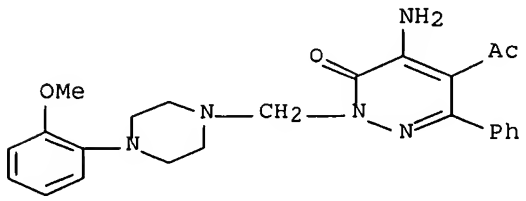
=> d l42 1-5 ibib ed ab hitstr hitind

L42  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:909005  HCAPLUS  Full-text
DOCUMENT NUMBER:          141:81614
TITLE:                    Comparison of MLR, PLS and GA-MLR in QSAR analysis
AUTHOR(S):                Saxena, A. K.; Prathipati, P.
CORPORATE SOURCE:         Med. Chem. Div., Cent. Drug Res. Inst., Lucknow,
                          226001, India
SOURCE:                   SAR and QSAR in Environmental Research (
                          2003), 14(5-6), 433-445
                          CODEN: SQERED; ISSN: 1062-936X
PUBLISHER:                Taylor & Francis Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  20 Nov 2003
AB   The use of the internet has evolved in quant. structure-activity relationship
     (QSAR) over the past decade with the development of web based activities like
     the availability of numerous public domain software tools for descriptor
     calcn. and chemometric toolboxes.  The importance of chemometrics in QSAR has
     accelerated in recent years for processing the enormous amount of information
     in form of predictive math. models for large datasets of mols.  With the
     availability of huge nos. of physicochem. and structural parameters, variable
     selection became crucial in deriving interpretable and predictive QSAR models.
```

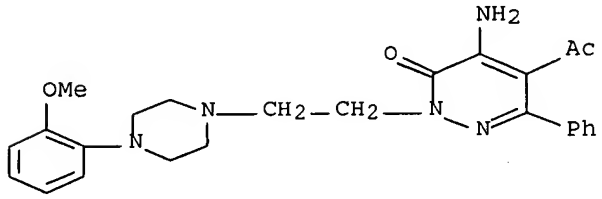
Among several approaches to address this problem, the principal component regression (PCR) and partial least squares (PLS) analyses provide highly predictive QSAR models but being more abstract, they are difficult to understand and interpret. Genetic algorithm (GA) is a stochastic method well suited to the problem of variable selection and to solve optimization problems. Consequently the hybrid approach (GA-MLR) combining GA with multiple linear regression (MLR) may be useful in derivation of highly predictive and interpretable QSAR models. In view of the above, a comparative study of stepwise-MLR, PLS and GA-MLR in deriving QSAR models for datasets of α1-adrenoreceptor antagonists and β3-adrenoreceptor agonists has been carried out using the public domain software Dragon for computing descriptors and free Matlab codes for data modeling.

IT **213483-34-2 213483-35-3 213483-36-4 213483-39-7**
(comparison of multiple linear regression, principal component regression and genetic algorithm-multiple linear regression in QSAR anal. of adrenoreceptor agonists and antagonists)

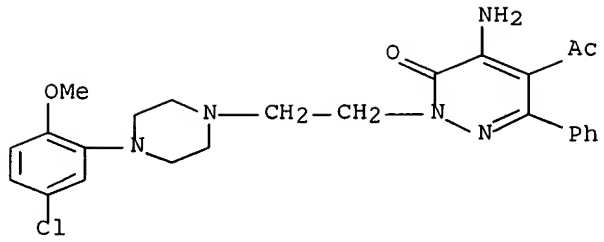
RN 213483-34-2 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[[4-(2-methoxyphenyl)-1-piperazinyl]methyl]-6-phenyl- (9CI) (CA INDEX NAME)



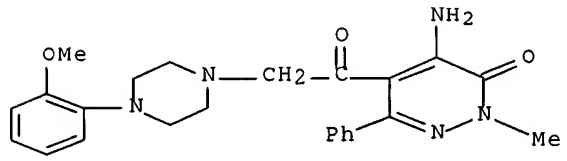
RN 213483-35-3 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-36-4 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-39-7 HCAPLUS
CN 3(2H)-Pyridazinone, 4-amino-5-[[4-(2-methoxyphenyl)-1-piperazinyl]acetyl]-2-methyl-6-phenyl- (9CI) (CA INDEX NAME)



CC 1-1 (Pharmacology)
IT 19216-56-9 102391-85-5 133399-66-3 134390-72-0 157396-51-5
159182-14-6 159182-18-0 159182-21-5 159182-26-0 159182-41-9
159182-43-1 159182-44-2 159182-45-3 159182-51-1 159182-52-2
159182-56-6 159182-62-4 159182-77-1 159182-79-3 159182-80-6
159182-81-7 159182-82-8 159182-91-9 159182-92-0 159182-93-1
159182-97-5 159182-98-6 159183-07-0 159183-09-2 159183-10-5
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213483-34-2 213483-35-3 213483-36-4
213483-39-7 234090-35-8 234090-36-9 234090-37-0
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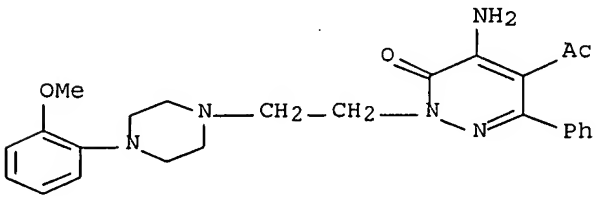
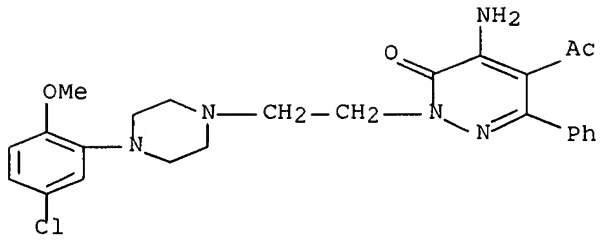
714950-98-8 714950-99-9 714951-00-5 714951-01-6 714951-02-7
714951-03-8 714951-04-9 714951-05-0 714951-07-2 714951-08-3
(comparison of multiple linear regression, principal component regression and genetic algorithm-multiple linear regression in QSAR anal. of adrenoreceptor agonists and antagonists)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

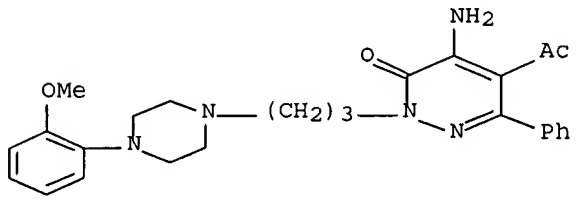
L42 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:343282 HCAPLUS Full-text
DOCUMENT NUMBER: 133:159627
TITLE: The ad hoc supermolecule approach to receptor ligand design
AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.
CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena e Reggio Emilia, Modena, 41100, Italy
SOURCE: THEOCHEM (**2000**), 503(1-2), 1-16
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 May 2000
AB Among the ligand design methods based on the theor. QSAR paradigm, the simple ad hoc supermol. approach is presented and applied to a highly non-congeneric set of α1-adrenergic receptor antagonists. The performance of the approach is satisfactory and highlights its (semi)quant. ligand design potentiality.
IT **213483-35-3 213483-36-4 213483-37-5**
(ad hoc supermol. approach to receptor ligand design)
RN 213483-35-3 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-36-4 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-37-5 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-6-phenyl- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)
Section cross-reference(s): 27, 28
IT 613-67-2 19216-56-9 67339-62-2 90402-40-7 94666-07-6
102993-22-6 139644-60-3 151563-49-4 152735-94-9 152736-76-0
152736-84-0 152753-37-2 169506-22-3 173059-05-7 173059-30-8
173059-39-7 173059-46-6 173059-47-7 173059-50-2 188018-68-0
213483-29-5 213483-30-8 213483-32-0 **213483-35-3**
213483-36-4 213483-37-5 288073-22-3 288073-23-4
(ad hoc supermol. approach to receptor ligand design)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

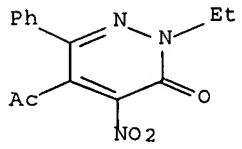
L42 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:262337 HCAPLUS Full-text
DOCUMENT NUMBER: 126:311728
TITLE: Novel Heterocyclic-Fused Pyridazinones as Potent and Selective Phosphodiesterase IV Inhibitors
AUTHOR(S): Dal iaz, Vittorio; Paola Giovannoni, Maria; Castellana, Carla; Palacios, Jose Maria; Beleta, Jorge; Domenech, Teresa; Segarra, Victor
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Florence, 50121, Italy
SOURCE: Journal of Medicinal Chemistry (**1997**), 40(10), 1417-1421
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:311728
ED Entered STN: 24 Apr 1997

AB A series of 6-aryl-4,5-heterocyclic-fused pyridazinones were designed and synthesized as selective phosphodiesterase (PDE) IV inhibitors. Biol. evaluation of these compds. demonstrated a good selectivity profile toward the PDE III family and exhibited greatly attenuated affinity for the Rolipram high-affinity binding site that seems to be responsible for undesirable side effects. Structure-activity relationships (SARs) studies showed that the presence of an Et group at pyridazine N-2 is associated with the best potency and selectivity profile.

IT **189306-94-3P 189306-96-5P 189306-97-6P**
(intermediate; preparation of novel heterocyclic-fused pyridazinones as potent and selective phosphodiesterase IV inhibitors)

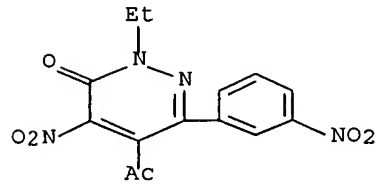
RN 189306-94-3 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-2-ethyl-4-nitro-6-phenyl- (9CI) (CA INDEX NAME)



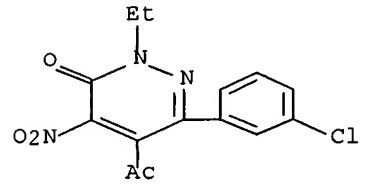
RN 189306-96-5 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-2-ethyl-4-nitro-6-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 189306-97-6 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-6-(3-chlorophenyl)-2-ethyl-4-nitro- (9CI) (CA INDEX NAME)

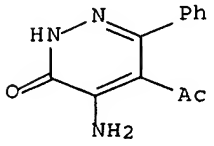


CC 1-3 (Pharmacology)
Section cross-reference(s): 28

IT 189306-87-4P 189306-88-5P 189306-89-6P 189306-90-9P
189306-91-0P 189306-92-1P 189306-93-2P **189306-94-3P**

189306-96-5P 189306-97-6P
(intermediate; preparation of novel heterocyclic-fused pyridazinones as potent and selective phosphodiesterase IV inhibitors)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:443310 HCAPLUS Full-text
DOCUMENT NUMBER: 89:43310
TITLE: Synthesis of pyrimido[4,5-d]pyridazin-8-one and -5-one
AUTHOR(S): Plescia, Salvatore; Dattolo, Gaetano; Sprio, Vincenzo
CORPORATE SOURCE: Italy
SOURCE: Atti della Accademia di Scienze, Lettere e Arti di Palermo, Parte 1: Scienze (**1976**), 34(2), 377-80
CODEN: AASLAN; ISSN: 0365-0448
DOCUMENT TYPE: Journal
LANGUAGE: Italian
ED Entered STN: 12 May 1984
AB Pyrimidopyridazinones I (R = Me, Ph, R1R2 = CMe:NCH:N) were obtained in 80-5% yield by cyclocondensation of I (R1 = Ac, R2 = NH2) with HCONH2. Reaction of I (R = Ph, R1 = NH2, R2 = Ac) with HCONH2 similarly gave I (R = Ph, R1R2 = N:CHN:CMe).
IT **17335-08-9**
(cyclocondensation of, with formamide)
RN 17335-08-9 HCAPLUS
CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-6-phenyl- (8CI, 9CI) (CA INDEX NAME)



CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 17334-69-9 17335-04-5 **17335-08-9**
(cyclocondensation of, with formamide)

L42 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:49558 HCAPLUS Full-text
DOCUMENT NUMBER: 68:49558
TITLE: Nitrogen heterocycles. II. Hydrogenation of isoxazolo[3,4-d]pyridazin-7-ones, isoxazolo[3,4-d]pyridazin-4-ones, and isoxazolo[3,4-d]pyridazine-4,7-diones
AUTHOR(S): Sprio, Vincenzo; Ajello, Enrico; Mazza, Acursio
CORPORATE SOURCE: Univ. Cagliari, Cagliari, Italy
SOURCE: Annali di Chimica (Rome, Italy) (**1967**), 57(7), 836-45
CODEN: ANCRAI; ISSN: 0003-4592
DOCUMENT TYPE: Journal
LANGUAGE: Italian

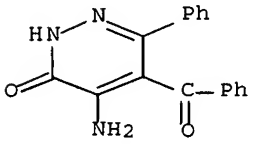
ED Entered STN: 12 May 1984

AB Hydrogenation of the title compds. gives 4-amino-5-acylpyridazine-3- ones, 4-amino-5-acylpyridazine-3,6-diones, and 5-amino-4-acylpyridazin- 3-ones. Thus, a cold solution of 0.01 mole of I, II, or III in 200 ml. EtOH was hydrogenated over Raney nickel in a Parr apparatus for 12 hrs. Filtration and concentration of the solution gives the products (IV-VI). Prepared were the following IV (R1, R2, and m.p. given): Me, Me, 234° (EtOH) [diacetyl derivative m. 202° (EtOH); oxime m. 249° (EtOH)]; Ph, Ph, 229-30° (EtOH) [acetyl derivative m. 197° (EtOH)]; Ph, Me, 201-3° (EtOH) [acetyl derivative m. 237° (EtOH)]. V decomposed 338°; VI m. 302° (EtOH) [oxime m. 242° (EtOH)]. Ir and N.M.R. spectra are given.

IT **17335-02-3P 17335-08-9P 19027-16-8P 19027-17-9P**
(preparation of)

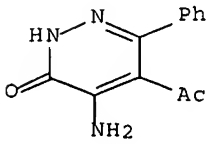
RN 17335-02-3 HCAPLUS

CN 3(2H)-Pyridazinone, 4-amino-5-benzoyl-6-phenyl- (8CI) (CA INDEX NAME)



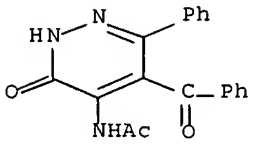
RN 17335-08-9 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-6-phenyl- (8CI, 9CI) (CA INDEX NAME)



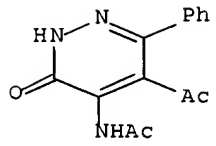
RN 19027-16-8 HCAPLUS

CN Acetamide, N-(5-benzoyl-2,3-dihydro-3-oxo-6-phenyl-4-pyridazinyl)- (8CI) (CA INDEX NAME)



RN 19027-17-9 HCAPLUS

CN Acetamide, N-(5-acetyl-2,3-dihydro-3-oxo-6-phenyl-4-pyridazinyl)- (8CI) (CA INDEX NAME)



CC 28 (Heterocyclic Compounds (More Than One Hetero Atom))
IT 17334-64-4P 17334-65-5P 17334-66-6P 17334-67-7P 17334-68-8P
17334-69-9P 17334-70-2P **17335-02-3P** 17335-03-4P
17335-04-5P 17335-05-6P 17335-06-7P **17335-08-9P**
19027-16-8P 19027-17-9P 19027-46-4P
(preparation of)

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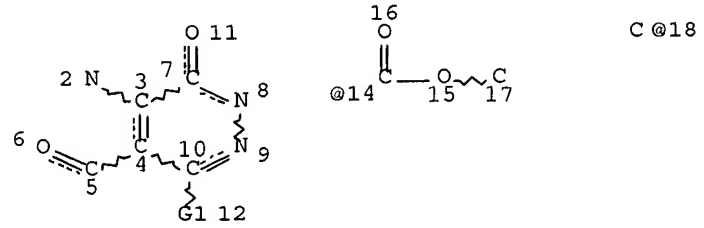
L9 STR



VAR G1=14/18
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L11	974	SEA	FILE=REGISTRY	SSS FUL	L9
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L18	77	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	DAL PIAZ, V?/AU
L19	4	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	AGUILAR IZQUIERDO, N?/AU
L20	9	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	BUIL ALBERO MARIA, A?/AU
L21	2	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	CARRASCAL RIERA, M?/AU
L22	10	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	GRACIA FERRER, J?/AU
L23	41	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	GIOVANNONI, M?/AU
L24	15	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	VERGELLI, C?/AU
L25	27	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L14 AND ((L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24))

=> d que l41

L32	0	SEA	AGUILAR IZQUIERDO, N?/AU		
L33	2	SEA	BUIL ALBERO MARIA, A?/AU		

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L34           0 SEA CARRASCAL RIERA, M?/AU
L35           2 SEA GRACIA FERRER, J?/AU
L36         113 SEA GIOVANNONI, M?/AU
L37          26 SEA VERGELLI, C?/AU
L38          35 SEA (L32 OR L33 OR L34 OR L35 OR L36 OR L37) AND (PYRIDAZIN
                ? AND INHIBITORS?)
L39         117 SEA DAL PIAZ, V?/AU
L40          35 SEA L39 AND (PYRIDAZIN? AND INHIBITORS?)
L41          39 SEA L38 OR L40


=> dup rem l25 l41
FILE 'HCAPLUS' ENTERED AT 11:19:51 ON 15 DEC 2006
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 11:19:51 ON 15 DEC 2006
PROCESSING COMPLETED FOR L25
PROCESSING COMPLETED FOR L41
L43          38 DUP REM L25 L41 (28 DUPLICATES REMOVED)
                ANSWERS '1-27' FROM FILE HCAPLUS
                ANSWERS '28-34' FROM FILE EMBASE
                ANSWER '35' FROM FILE BIOSIS
                ANSWERS '36-38' FROM FILE MEDLINE

=> d l43 1-38 ibib ab

L43  ANSWER 1 OF 38  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER:        2002:815783  HCAPLUS  Full-text
DOCUMENT NUMBER:         138:378543
TITLE:                   Synthesis and evaluation of some
                         pyrazolo[3,4-d]pyridazinones and analogues as PDE
                         5 inhibitors potentially useful as peripheral
                         vasodilator agents
AUTHOR(S):               Dal Piaz, Vittorio; Castellana, Maria
                         Carla; Vergelli, Claudia;
                         Giovannoni, Maria Paola; Gavalda, Amadeu;
                         Segarra, Victor; Beleta, Jorge; Ryder, Hamish;
                         Palacios, Jose Maria
CORPORATE SOURCE:        Dipartimento di Scienze Farmaceutiche, Florence,
                         50121, Italy
SOURCE:                  Journal of Enzyme Inhibition and Medicinal
                         Chemistry (2002), 17(4), 227-233
                         CODEN: JEIMAZ; ISSN: 1475-6366
PUBLISHER:               Taylor & Francis Ltd.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
OTHER SOURCE(S):         CASREACT 138:378543
AB    A series of pyrazolo[3,4-d]pyridazinones and analogs, potentially useful as
      peripheral vasodilators, were synthesized and evaluated as inhibitors of PDE5
      extracted from human platelets. Several of them showed IC50 values in the
      range 0.14-1.4 μM. A good activity and selectivity profile vs. PDE6 was found
      for compound (6-benzyl-3-methyl-1- isopropyl-4-phenylpyrazolo[3,4-d]
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pyridazin-7(6H)-one). Structure-activity relationship studies demonstrated the essential role played by the benzyl group at position-6 of the pyrazolopyridazine system. Other types of pyridazinones fused with five and six membered heterocycles (pyrrole, isoxazole, pyridine and dihydropyridine), as well as some open models were prepared and evaluated. Besides the pyrazole, the best fused systems proved to be isoxazole and pyridine.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2002:154884 HCAPLUS Full-text
DOCUMENT NUMBER: 137:362487
TITLE: Isoxazolo[3,4-d]pyridazinones and analogues as Leishmania mexicana PDE inhibitors
AUTHOR(S): **Dal Piaz, Vittorio**; Rascon, A.; Dubra, M. E.; **Giovannoni, M. P.**; **Vergelli, C.**; Castellana, M. C.
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universite Firenze, Florence, 50121, Italy
SOURCE: Farmaco (2002), 57(2), 89-96
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of isoxazolopyridazinones and analogs has been prepared and evaluated as Leishmania mexicana phosphodiesterase (PDE) inhibitors. Some of the synthesized compds. showed a moderate PDE inhibitory activity at 100 μM and preliminary structure-activity relationships were discussed.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1999:304425 HCAPLUS Full-text
DOCUMENT NUMBER: 130:352238
TITLE: Isoxazolo-[3,4-d]-pyridazin-7-(6H)-one as a potential substrate for new aldose reductase inhibitors
AUTHOR(S): Costantino, Luca; Rastelli, Giulio; Gamberini, M. Cristina; **Giovannoni, M. Paola**; **Dal Piaz, Vittorio**; Vianello, Paola; Barlocco, Daniela
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Via G. Campi 183, Modena, 41100, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(11), 1894-1900
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The isoxazolo[3,4-d]pyridazin-7(6H)-one I (R = Ph, Me, 4-ClC6H4, etc.) and its corresponding open derivs. 5-acetyl-4-amino(4-nitro)-6- substituted-3(2H)-pyridazinones II (X = NH2, NO2) were used as simplified substrates for the synthesis of new aldose reductase inhibitors with respect to the previously reported 5,6-dihydrobenzo[h]cinnolin-3(2H)-one-2 acetic acid III. Moreover, a few derivs. lacking the 5-acetyl group were prepared Several compds. derived from I displayed inhibitory properties comparable to those of Sorbinil. In this class the presence at position 6 of a Ph carrying an electron-withdrawing substituent proved to be beneficial, independently from its position on the

ring I [R = 4-ClC6H4, 2-, 3-, 4-O2NC6H4, R' = (CH2)nCO2H, n = 1]. Acetic acid derivs. were more effective than propionic and butyric analogs. On the contrary, all the monocyclic compds. IV (R = Ph, Me, n = 1-3), V (R = Ph, CH2Ph, 4-ClC6H4, etc.), and VI (R = H, CH2Ph, CH2CH2Ph, CH2CH2-pyrid-2-yl) were either inactive or only weakly active. The 3-methyl-4-(p-chlorophenyl)isoxazolo[3,4-d]pyridazin-7(6H)-one acetic acid, which proved to be the most potent derivative, was also investigated in mol. modeling studies, to assess possible similarities in its interaction with the enzyme, with respect to the model III.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1998:793835 HCAPLUS Full-text
DOCUMENT NUMBER: 130:162741
TITLE: Heterocyclic-fused 3(2H)-pyridazinones as potent and selective PDE IV inhibitors: further structure-activity relationships and molecular modeling studies
AUTHOR(S): **Dal Piaz, Vittorio**; Paola Giovannoni, Maria; Castellana, Carla; Palacios, Jose Maria; Beleta, Jorge; Domenech, Teresa; Segarra, Victor
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Florence, 50121, Italy
SOURCE: European Journal of Medicinal Chemistry (1998), 33(10), 789-797
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel group of heterocyclic-fused 3(2H)-pyridazinones were synthesized and evaluated as PDE III and PDE IV inhibitors and their affinity for 3H Rolipram high affinity binding site was determined The obtained data demonstrated that some of the new compds. are endowed with potent and selective PDE IV inhibitory activity and greatly attenuated affinity for the Rolipram high affinity binding site that seems to be responsible for unwanted effects. Theor. calcns., performed on representative compds., demonstrated the presence of three hydrogen-bonding acceptor regions, of which one looks quite different with respect to literature compds. This finding could explain the different pharmacol. profile of the title compds. with respect to the analogs reported in the literature.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1997:508095 HCAPLUS Full-text
DOCUMENT NUMBER: 127:214587
TITLE: Synthesis of 4,5-functionalized-2-methyl-6-(substituted aryl)-3(2H)-pyridazinones: a new group of potent platelet aggregation inhibitors
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Farmaco (1997), 52(3), 173-178
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Societa Chimica Italiana
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:214587
AB A series of 4,5-functionalized-2-methyl-6-(substituted phenyl)-3(2H)-pyridazinones were synthesized and evaluated as platelet aggregation inhibitors in human platelet rich plasma (PRP). The new products generally displayed significant higher activity with respect to the corresponding unsubstituted aryl compds. Several compds. appeared to be of particular interest with IC50s in the submicromolar range. Structure-activity relationships (SARs) are discussed.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11
ACCESSION NUMBER: 1996:732957 HCAPLUS Full-text
DOCUMENT NUMBER: 126:84307
TITLE: Synthesis and evaluation as platelet aggregation inhibitors of 6-phenyl-2,4-substituted-3(2H)-pyridazinones and their rigid analogs benzo[h]cinnolin-3,5-diones
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**; Franconi, Flavia
CORPORATE SOURCE: Dip. Scienze Farmaceutiche, Univ. Firenze, 50121, Italy
SOURCE: Drug Design and Discovery (1996), 14(1), 53-75
CODEN: DDDIEV; ISSN: 1055-9612
PUBLISHER: Harwood
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 5-acyl-6-phenyl-2,4-substituted-3(2H)-pyridazinones and analogous benzo[h]cinnolin-3,5-diones with reduced flexibility has been prepared and evaluated as human platelet aggregation inhibitors. The 4-methylsulfoxide I was the most potent compound of the series (IC50 = 1.2 μM). SAR studies have shown the primary importance of an electroneg. substituent at position 4 and an acetyl group at position 5 of the pyridazine system for potent platelet aggregation inhibitory activity. Biol. tests performed on a group of representative compds. showed that these products have no effects on prostaglandins, thromboxanes, and nitric oxide biosynthetic pathways. Some of synthesized compds. produced a moderate increase of cAMP level in platelets which does not depend on adenylate cyclase stimulation. Tests performed on human platelet phosphodiesterase III have shown that these compds. are not inhibitors of this enzyme.

L43 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 1994:645151 HCAPLUS Full-text
DOCUMENT NUMBER: 121:245151
TITLE: 4-substituted-5-acetyl-2-methyl-6-phenyl-3(2H)pyridazinones as PGE2 and IL-1 release inhibitors from mouse adherent macrophages
AUTHOR(S): **Dal Piaz, V.**; **Giovannoni, M. P.**; Ciciani, G.; Becherucci, C.; Parente, L.
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SOURCE: Pharmacological Research (1994), 29(4), 367-72
CODEN: PHMREP; ISSN: 1043-6618
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 4,5-functionalized 3(2H)-pyridazinones (I, R = NO2, NH2, Br, SOMe) were evaluated as PGE2 and interleukin-1 (IL-1) release inhibitors from mouse

adherent macrophages. Among the tested compds. only I (R = NH2) was devoid of activity in both the PGE2 and IL-1 tests, whereas the other compds., showed a significant dose-dependent activity. I (R = NO2, Br or SOMe) inhibited PGE2 better than IL-1 release from stimulated macrophages. I (R = SOMe), which showed an IC50=5.5 μM in the IL-1 test, appears to be a promising agent in this cell inflammation model. Structure-activity relation studies demonstrated the importance of the presence of a substituent characterized by a pos. σ constant at position 4 of the pyridazine system.

L43 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 1991:441291 HCAPLUS Full-text
DOCUMENT NUMBER: 115:41291
TITLE: 5-Acyl-6-aryl-4-nitro-3(2H)pyridazinones and related 4-amino compounds: synthesis and pharmacological evaluation
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Turco, Giovanni; **Giovannoni, Maria Paola**; Miceli, Mauro; Pirisino, Renato; Perretti, Mauro
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy
SOURCE: Journal of Pharmaceutical Sciences (1991), 80(4), 341-8
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several 4-nitro- and 4-amino-5-acyl-6-acyl-3(2H)-pyridazinones were prepared and their in vitro and ex vivo antiaggregatory properties were evaluated. 4-Nitro derivs. generally showed good activity in vitro towards arachidonic acid (AA)-induced human blood platelet aggregation. The 4-amino compound (I, R1 = R3 = Me; R2 = Ph; R4 = NH2) which has weak in vitro activity, exhibited antiplatelet activity, particularly on adenosine dephosphate (ADP)-induced aggregation ex vivo in rabbit. Moreover, the same compound was active in platelet-activating factors (PAF)-induced rat paw hyperalgesia and to be endowed with low acute oral toxicity. The 4-amino derivs. and the other pyridazinones administered orally to rats were also more potent anti-inflammatory agents than acetylsalicylic acid. I (R1 = R3 = Me; R2 = Ph; R4 = NO2 or NH2) tested in vitro on lipopolysaccharide (LPS)-stimulated rat peritoneal macrophages, were active in the inhibition of prostaglandin E2 (PGE2) production and interleukin-1 activity. Structure-activity relation studies in the series of antiaggregating pyridazinones showed the primary importance of the nitro and acetyl substituents at positions 4 and 5, resp. Hydrophobic substituents at position 2 were also required for better activity.

L43 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1354871 HCAPLUS Full-text
DOCUMENT NUMBER: 144:88299
TITLE: Preparation of pyridazin-3(2H)-one derivatives as PDE4 inhibitors for the treatment of pathological diseases
INVENTOR(S): **Aguilar Izquierdo, Nuria**; **Carrascal Riera, Marta**; **Dal Piaz, Vittorio**; **Gracia Ferrer, Jordi**; Lumeras Amador, Wenceslao; Masdeu Margalef, Maria del Carmen; Warrellow, Graham
PATENT ASSIGNEE(S): Almirall Prodesfarma, S.A., Spain
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005123693	A1	20051229	WO 2005-EP6712	20050621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2251867	A1	20060501	ES 2004-1512	20040621
PRIORITY APPLN. INFO.:			ES 2004-1512 A	20040621

OTHER SOURCE(S): MARPAT 144:88299

AB The invention relates to new therapeutically useful pyridazin-3(2H)-one derivs. I [wherein R1 = H or (un)substituted alk(en/yn)yl; R2 = (un)substituted heteroaryl; R3 = H, alkyl aryl, etc., R4 = (un)substituted (hetero)aryl, and pharmaceutically acceptable salts or N-oxides thereof], to their prepns., and to pharmaceutical compns. containing them. These compds. are potent inhibitors of phosphodiesterase 4 (PDE4), and are thus useful in the treatment, prevention or suppression of pathol. conditions, diseases and disorders known to be susceptible of being improved by inhibition of PDE4, such as asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease. For example, II, which had an IC50 of 0.07 nM in the PDE4 inhibition assay, was synthesized by esterification of the corresponding acid (preparation given) with chloromethyl pivalate.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1350734 HCAPLUS Full-text
DOCUMENT NUMBER: 144:88298
TITLE: Preparation of pyridazin-3(2H)-one derivatives as PDE4 inhibitors for the treatment of pathological diseases
INVENTOR(S): **Buil Albero, Maria Antonia**; **Dal Piaz, Vittorio**; Garrido Rubio, Yolanda; **Gracia Ferrer, Jordi**; Pages Santacana, Lluis Miquel; Taltavull Moll, Joan
PATENT ASSIGNEE(S): Almirall Prodesfarma, SA, Spain
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005123692 A1 20051229 WO 2005-EP6304 20050613
WO 2005123692 C1 20060504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
ES 2251866 A1 20060501 ES 2004-1500 20040618
PRIORITY APPLN. INFO.: ES 2004-1500 A 20040618

OTHER SOURCE(S): MARPAT 144:88298

AB The invention relates to new therapeutically useful pyridazin-3(2H)-one derivs. I [wherein R1 = H or (un)substituted alk(en/yn)yl; R2 = (un)substituted heteroaryl; R3 = H or alkylcarbonyl; R4 = H, alkyl, aryl, etc., and pharmaceutically acceptable salts or N-oxides thereof], to their prepns., and to pharmaceutical compns. containing them. These compds. are potent inhibitors of phosphodiesterase 4 (PDE4), and are thus useful in the treatment, prevention or suppression of pathol. conditions, diseases and disorders known to be susceptible of being improved by inhibition of PDE4, such as asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease. For example, II, which had an IC50 of 0.36 nM in the PDE4 inhibition assay, was synthesized by esterification of the corresponding acid (preparation given) with chloromethyl 2,2-dimethylbutyrate.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:472131 HCAPLUS Full-text
DOCUMENT NUMBER: 143:26620
TITLE: Preparation of pyridazin-3(2H)-ones and their use as PDE4 inhibitors
INVENTOR(S): **Dal Piaz, Vittorio**; **Aguilar Izquierdo, Nuria**; **Buil Albero, Maria Antonia**; Garrido Rubio, Yolanda; **Giovannoni Maria, Paola**; **Gracia Ferrer, Jordi**; Lumeras Amador, Wenceslao; **Vergelli, Claudia**
PATENT ASSIGNEE(S): Almirall Prodesfarma, S. A., Spain
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049581	A1	20050602	WO 2004-EP12604	20041108
WO 2005049581	C1	20060504		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL,
PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

ES 2232306	A1	20050516	ES 2003-2613	20031110
ES 2232306	B1	20060801		
AU 2004291282	A1	20050602	AU 2004-291282	20041108
CA 2545193	AA	20050602	CA 2004-2545193	20041108
EP 1682519	A1	20060726	EP 2004-797700	20041108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
CN 1878759	A	20061213	CN 2004-80033113	20041108
NO 2006002726	A	20060612	NO 2006-2726	20060612

PRIORITY APPLN. INFO.: ES 2003-2613 A 20031110
WO 2004-EP12604 W 20041108

OTHER SOURCE(S): MARPAT 143:26620

AB Title compds. I [R1-2 = H, acyl, alkoxycarbonyl, etc.; R3 = mono/polycyclic (hetero)aryl, etc.; R4 = H, OH, alkoxy, amino, etc.; R5 = carboxy, mono/polycyclic (hetero)aryl, etc.] are prepared For instance, 1-Ethyl-3-(4-fluorophenyl)-6-oxo-5-((pyridin-3-yl)amino)-1,6- dihydropyridazine-4-carbonitrile (II) is prepared from 5-Amino-1-ethyl-3-(4-fluorophenyl)-6-oxo-1,6-dihydropyridazine-4- carbonitrile (preparation given) and 3-bromopyridine. II has IC50 = 5.4 for PDE4. I are useful for the treatment of asthma, COPD, etc.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:565225 HCAPLUS Full-text
DOCUMENT NUMBER: 141:106481
TITLE: Preparation of pyridazin-3(2H)-ones as Phosphodiesterase 4 (PDE4) inhibitors
INVENTOR(S): **Dal Piaz, Vittorio; Aguilar Izquierdo, Nuria; Buil Albero Maria, Antonia; Carrascal Riera, Marta; Gracia Ferrer, Jordi; Giovannoni, Maria Paola; Vergelli, Claudia**
PATENT ASSIGNEE(S): Almirall Prodesfarma Sa, Spain
SOURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058729	A1	20040715	WO 2003-EP14722	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,				

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

ES 2211344	A1	20040701	ES 2002-3003	20021226
ES 2211344	B1	20051001		
CA 2512099	AA	20040715	CA 2003-2512099	20031222
AU 2003290110	A1	20040722	AU 2003-290110	20031222
EP 1575926	A1	20050921	EP 2003-782471	20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016883	A	20051025	BR 2003-16883	20031222
CN 1753876	A	20060329	CN 2003-80109897	20031222
JP 2006515302	T2	20060525	JP 2004-562819	20031222
NO 2005003614	A	20050926	NO 2005-3614	20050725
US 2006173008	A1	20060803	US 2005-539821	20051214
PRIORITY APPLN. INFO.:			ES 2002-3003 A	20021226
			WO 2003-EP14722 W	20031222

OTHER SOURCE(S): MARPAT 141:106481

AB Title compds. I [wherein R1, R2 = independently H, acyl, hydroxycarbonyl, alkoxycarbonyl, monoalkyl/dialkyl/carbamoyl, (un)substituted alk(en/yn)yl, hetero/aryl, (un)saturated heterocyclyl, etc.; R3 = (un)substituted monocyclic or plycyclic hetero/aryl; R5 = (un)substituted alkoxycarbonyl, monocyclic or plycyclic hetero/aryl; R4 = H, OH and derivs., NH2 and derivs., (un)substituted alk(en/yn)yl, etc.; and their N-oxides and pharmaceutically acceptable salts] were prepare as potent and selective inhibitors of Phosphodiesterase 4 (PDE4). Four pharmaceutical compns. are given. For example, II was prepared by hydrogenation of 5-acetyl-4-amino-2-ethyl-6-(pyridin-3- yl)pyridazin-3(2H)-one over Pd/C in ethanol, and reaction of the amine with 3-fluorophenylboronic acid in the presence of Cu(OAc)2/TEA/mol. sieves/CH2Cl2. Preffered I exhibited an IC50 value < 30 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

L43 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:931340 HCAPLUS Full-text
DOCUMENT NUMBER: 140:5060
TITLE: Preparation of pyridazin-3(2H)-ones as Phosphodiesterase 4 (PDE4) inhibitors
INVENTOR(S): **Dal Piaz, Vittorio; Giovannoni, Maria Paola; Vergelli, Claudia; Aguilar, Izquierdo Nuria**
PATENT ASSIGNEE(S): Almirall Prodesfarma Sa, Spain; Aguilar Izquierdo, Nuria
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003097613	A1	20031127	WO 2003-EP5056		20030514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
ES 2195785	A1	20031201	ES 2002-1111		20020516
ES 2195785	B1	20050316			
CA 2485896	AA	20031127	CA 2003-2485896		20030514
AU 2003236648	A1	20031202	AU 2003-236648		20030514
EP 1503992	A1	20050209	EP 2003-735387		20030514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003010106	A	20050222	BR 2003-10106		20030514
JP 2005533024	T2	20051104	JP 2004-505346		20030514
NZ 536604	A	20060728	NZ 2003-536604		20030514
ZA 2004009173	A	20050729	ZA 2004-9173		20041111
NO 2004005461	A	20050119	NO 2004-5461		20041215
US 2006052379	A1	20060309	US 2005-513219		20050629
PRIORITY APPLN. INFO.:			ES 2002-1111	A	20020516
			WO 2003-EP5056	W	20030514

OTHER SOURCE(S): MARPAT 140:5060

AB Title compds. I [wherein R1 = H, acyl, alkoxycarbonyl, monoalkyl/dialkyl/carbamoyl, (un)substituted alkyl, (CH2)n-R6; n = 0 to 4; R6 = cycloalkyl, (un)substituted aryl, 3- to 7-membered heterocyclyl; R2 = R1, (un)substituted alkyl; R3, R5 = independently (un)substituted monocyclic or bicyclic aryl; R4 = H, OH and derivs., NH2 and derivs., (un)substituted alkyl, (CH2)n-R6; with the proviso that when R2 = H and R3, R4 = unsubstituted Ph, R1 is not methyl; and their pharmaceutical acceptable salts] were prepare as potent and selective inhibitors of Phosphodiesterase 4 (PDE4). Four pharmaceutical compns. are given. For example, II was prepared by hydrogenation of 6-ethyl-3-methyl-4-phenylisoxazolo[3,4-d]pyridazin- 7(6H)-one over Pd/C in ethanol, and reaction of the resulting 4-aminopyridazinone with 3-fluorophenylboronic acid in the presence of Cu(OAc)2/TEA/mol. sieves/CH2Cl2. Selected I exhibited an IC50 value < 20 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:829129 HCAPLUS Full-text

DOCUMENT NUMBER: 140:357279

TITLE: 4-Amino-3(2H)-pyridazinones bearing arylpiperazinylalkyl groups and related compounds: synthesis and antinociceptive activity

AUTHOR(S): **Dal Piaz, Vittorio; Vergelli,**

Claudia; Giovannoni, Maria Paola; Scheideler, Mark A.; Petrone, Giuseppe; Zaratin, Paola

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy

SOURCE: Farmaco (2003), 58(11), 1063-1071
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:357279

AB A series of 4-amino-3(2H)-pyridazinones substituted at position 2 with arylpiperazinylalkyl groups and analogs were synthesized and their antinociceptive effect was evaluated in the mouse abdominal constriction model. Preliminary SARs studies were performed. Several of the novel compds. dosed at 100 mg/kg s.c. significantly reduced the number of writhes induced by the noxious stimulus. Compound I showed 100% inhibition of writhes and was able to protect all the treated animals from the effect of the chemical stimulus. Subsequent dose-response studies revealed I to be almost 40-fold more potent than the structurally related Emorfazone.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:435617 HCAPLUS Full-text
DOCUMENT NUMBER: 135:180739
TITLE: Phenylpiperazinylalkylamino Substituted Pyridazinones as Potent α1 Adrenoceptor Antagonists
AUTHOR(S): Barlocco, Daniela; Cignarella, Giorgio; **Dal Piaz, Vittorio; Giovannoni, M. Paola** ; De Benedetti, Pier G.; Fanelli, Francesca; Montesano, Federica; Poggesi, Elena; Leonardi, Amedeo
CORPORATE SOURCE: Istituto Chimico Farmaceutico e Tossicologico, Milan, 20131, Italy

SOURCE: Journal of Medicinal Chemistry (2001), 44(15), 2403-2410
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB QSAR models have been used for designing a series of compds. characterized by a N-phenylpiperazinylalkylamino moiety linked to substituted pyridazinones, which have been synthesized. Measurements of the binding affinities of the new compds. toward the α1a-, α1b-, and α1d-AR cloned subtypes as well as the 5-HT1A receptor have been done validating, at least in part, the estns. of the theor. models. This study provides insight into the structure activity relationships of the α1-ARs ligands and their α1-AR/5-HT1A selectivity.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:566668 HCAPLUS Full-text
DOCUMENT NUMBER: 131:286474
TITLE: New synthesis of differently fused pyridazinoquinolines

AUTHOR(S): **Dal Piaz, Vittorio; Giovannoni, Maria Paola;** Ciciani, Giovanna; **Vergelli, Claudia**
CORPORATE SOURCE: Dipartimento Scienze Farmaceutiche, Univ. Firenze, Florence, I-50121, Italy
SOURCE: Synlett (1999), (9), 1453-1455
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:286474
AB Treatment of 4-chloro- and 4-(methylthio)-5-acetyl-2-methyl-6-(2-nitrophenyl)-3(2H)-pyridazinone with SnCl2/HCl afforded pyridazino[4,3-c]quinolinones, whereas a pyridazino[4,5-b]quinolinone was prepared by reduction of 5-acetyl-4-anilino-6-phenyl-3(2H)-pyridazinone with NaBH4, followed by dehydration with polyphosphoric acid.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:542409 HCAPLUS Full-text
DOCUMENT NUMBER: 129:260414
TITLE: Isoxazolo[3,4-d]pyridazin-7(6H)-ones and their corresponding 4,5-disubstituted-3-(2H)-pyridazinone analogs as new substrates for α1-adrenoceptor selective antagonists: synthesis, modeling, and binding studies
AUTHOR(S): Montesano, Federica; Barlocco, Daniela; **Dal Piaz, Vittorio;** Leonardi, Amedeo; Poggesi, Elena; Fanelli, Francesca; De Benedetti, Piero G.
CORPORATE SOURCE: 1st. Chimica Farmaceutica e Tossicologica, Milan, 20131, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(7), 925-935
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of phenylpiperazinylalkyl moieties were attached to monocyclic or bicyclic substituted pyridazinones and the new compds. tested for their affinity towards α1-adrenoceptor and its α1a, α1b and α1d subtypes, as well as serotonin 5-HT1A receptor. Several analogs showed remarkable potency and selectivity towards α1a, and α1d with respect to α1b subtype. None of the test compds. exhibited significant affinity for 5-HT1A receptor. Finally, on the basis of the α1-AR subtypes 3D models recently proposed, we have elaborated theor. interaction models for the new compds. The theor. study allowed us to predict the affinity of the new compds. as well as to infer the structural/dynamics determinants of their interaction with the three α1-AR subtypes.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:137308 HCAPLUS Full-text
DOCUMENT NUMBER: 124:289447
TITLE: 4,5-Functionalized 6-phenyl-3(2H)-pyridazinones: synthesis and evaluation of antinociceptive

activity
AUTHOR(S): **Dal Piaz, V.; Giovannoni, M. P.** ; Ciciani, G.; Barlocco, D.; Giardina, G.; Petrone, G.; Clarke, G. D.
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy
SOURCE: European Journal of Medicinal Chemistry (1996), 31(1), 65-70
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2-Substituted 4,5-functionalized 6-phenyl-3(2H)-pyridazinones were synthesized and their antinociceptive activities were evaluated in the mouse abdominal constriction model. Single dose studies showed that compds. I and II were more active than the reference drug, Emorfazone, in inhibiting the effects of the noxious chemical stimulus, p-phenylquinone. Subsequent dose-response studies revealed I to be almost seven-fold more potent than Emorfazone.

L43 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:534061 HCAPLUS Full-text
DOCUMENT NUMBER: 121:134061
TITLE: 5-Acetyl-2-methyl-4-nitro-6-phenyl-3(2H)-pyridazinone: versatile precursor to hetero-condensed pyridazinones
AUTHOR(S): **Dal Piaz, V.**; Ciciani, G.; **Giovannoni, M. P.**
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy
SOURCE: Synthesis (1994), (7), 669-71
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:134061
AB Title compound I is a very useful intermediate for the synthesis five- and six-membered hetero-condensed pyridazinones, e.g., thienopyridazinone II and pyridopyridazinone III, in high yields under generally mild and simple reaction conditions.

L43 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:435499 HCAPLUS Full-text
DOCUMENT NUMBER: 121:35499
TITLE: Synthesis and evaluation of some 4,5-disubstituted 6-phenyl-3(2H)-pyridazinones as hypotensive agents
AUTHOR(S): **Dal Piaz, V.; Giovannoni, M. P.** ; Laguna, R.; Cano, E.
CORPORATE SOURCE: Dip. Sci. Farm., Florence, 50121, Italy
SOURCE: European Journal of Medicinal Chemistry (1994), 29(3), 249-52
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synthesis of the title compds. I (X = amino, nitro, methylthio, etc.; R = H, alkyl) was described. I were tested for hypotensive activity in normotensive rats.

L43 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:213001 HCAPLUS Full-text
DOCUMENT NUMBER: 118:213001
TITLE: Diels-Alder reactions on 5-acetyl-2-methyl-4-nitro-6-phenylpyridazin-3(2H)-one: a new facet of the pyridazine system
AUTHOR(S): **Dal Piaz, Vittorio; Giovannoni, Maria P.**; Ciciani, Giovanna; Giomi, Donatella; Nesi, Rodolfo
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Florence, Florence, I-50121, Italy
SOURCE: Tetrahedron Letters (1993), 34(1), 161-2
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:213001
AB The title nitro ketone I was shown to react with 2,3-dimethylbuta-1,3- diene and cyclohexa-1,3-diene affording a mixture of the phthalazones II (R = NO2, R1 = H; RR1 = bond) and the pyridazinone III, resp., through [2+4] cycloaddn. processes.

L43 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:656096 HCAPLUS Full-text
DOCUMENT NUMBER: 115:256096
TITLE: Isoxazolo[3,4-d]pyridazin-7(6H)-ones. Synthesis of 3-unsubstituted derivatives: a reinvestigation
AUTHOR(S): **Dal Piaz, V.**; Ciciani, G.; **Giovannoni, M. P.**
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy
SOURCE: Tetrahedron Letters (1991), 32(27), 3229-30
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isoxazole I (R = CO2Et, R1 = COPh, R2 = H) condensed with MeNHNH2 or MeNHNH2/polyphosphoric acid to give I (RR1 = CONMeN:CH, R2 = Ph; RR1 = CONMeN:CPh, R2 = H; resp.), which underwent catalytic hydrogenation to give pyridazinones II (R3 = H, R4 = COPh; R3 = Ph, R4 = CHO, resp.).

L43 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:583222 HCAPLUS Full-text
DOCUMENT NUMBER: 115:183222
TITLE: Reductive cleavage of isoxazolo[3,4-d]pyridazinones: a synthetic approach to various 4,5-functionalized 3(2H)-pyridazinones
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Florence, Florence, 50121, Italy
SOURCE: Heterocycles (1991), 32(6), 1173-9
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:183222
AB 4-Aminopyridazinones I (R = H, Me, Ph; R1 = H, Me) were obtained in good yields by reductive ring opening of the isoxazole ring of isoxazolo[3,4-d]pyridazinones II. Starting from Et 4-acylisoxazole-3-carboxylates III (R1 = H, Me), several pyridazinones IV (R = H, Me, Ph) are obtained in one step by treatment with RNHNH2 and Pd/C.

L43 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:6499 HCAPLUS Full-text
DOCUMENT NUMBER: 116:6499
TITLE: Synthesis and evaluation of in vitro antitumor activity of some substituted 5-pyridazinyl-styrylketones
AUTHOR(S): Ciciani, Giovanna; **Dal Piaz, Vittorio**; **Giovannoni, Maria Paola**
CORPORATE SOURCE: Fac. Farm., Univ. Florence, Florence, 50121, Italy
SOURCE: Farmaco (1991), 46(7-8), 873-85
CODEN: FRMCE8; ISSN: 0014-827X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isoxazolopyridazinone I (R = R1 = H) reacted with 4-R2C6H4CHO (R2 = H, OMe, Cl, F) to give I (RR1 = CHC6H4R2-4) (II). Treatment of acetylnitrophenylpyridazinone III (R = R1 = H, R3 = NO2) with amines (morpholine, pyrrolidine, piperidine, diethylamine, 2-methylaziridine) gave III [R3 = 4-morpholinyl, 1-pyrrolidinyl, 1-piperidinyl, diethylamino, 1-(2-methylaziridinyl)] which react with 4-R2C6H4CHO to give III (RR1 = CHC6H4R2-4) (IV). The antitumor activity of II and IV were measured against 60 human tumor cell lines.

L43 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:178836 HCAPLUS Full-text
DOCUMENT NUMBER: 112:178836
TITLE: New synthetic approach to pyrazolo[3,4-d]pyridazin-7(6H)-one ring system
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**; Turco, Giovanni
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy
SOURCE: Heterocycles (1989), 29(8), 1595-600
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:178836
AB Treatment of 2,6-disubstituted 5-acetyl-4-nitropyridazin-3(2H)-ones I (R = Me, Ph) with hydrazine or substituted hydrazines in alc. medium gives rise in high yields to new 1H- and 2H-pyrazolo[3,4-d]pyridizin- 7(6H)-ones II and III (R1 = H, Me).

L43 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:477947 HCAPLUS Full-text
DOCUMENT NUMBER: 111:77947
TITLE: Oxidative cleavage of 7-oxo-6,7-dihydroisoxazolo[3,4-d]pyridazines by cerium(IV) diammonium nitrate. A synthetic approach to new 5-acyl-4-nitro-3-oxo-2,3-dihydropyridazines
AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Turco, Giovanni
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy
SOURCE: Synthesis (1989), (3), 213-14
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:77947

AB Treatment of oxodihydroisoxazolopyridazines I (R = Me, Ph, cyclohexyl; R1 = Me, Ph; R2 = Me, Et) with Ce(NH4)2(NO3)6 in an AcOH-H2O mixture containing HNO3 gave 30-53% acylnitrooxodihydropyridazines II (same R-R2).

L43 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:213879 HCAPLUS Full-text

DOCUMENT NUMBER: 106:213879

TITLE: Pyrazolo[1',5':1,6]pyrimido[4,5-d]pyridazin-7(8H)-one: a new heterocyclic ring system from isoxazolopyridazinones

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Chimichi, Stefano

CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy

SOURCE: Heterocycles (1986), 24(11), 3143-8
CODEN: HTCYAM; ISSN: 0385-5414

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 106:213879

AB Treatment of isoxazolopyridazinones I (R = H, Me; R1 = Me, Ph; R2 = Ph, 4-ClC6H4) with N2H4 afforded the pyrazole derivs. II which were converted in high yields into the new pyrazolopyrimidopyridazinones III by ring-closure with Ac2O.

L43 ANSWER 28 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2006401269 EMBASE Full-text

TITLE: Novel pyrazolopyrimidopyridazinones with potent and selective phosphodiesterase 5 (PDE5) inhibitory activity as potential agents for treatment of erectile dysfunction.

AUTHOR: **Giovannoni M.P.**; **Vergelli C.**; Biancalani C.; Cesari N.; Graziano A.; Biagini P.; Gracia J.; Gavalda A.; **Dal Piaz V.**

CORPORATE SOURCE: M.P. Giovannoni, Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Via Ugo Schiff 6, Sesto Fiorentino, 50019 Firenze, Italy. mariapaola.giovannoni@unifi.it

SOURCE: Journal of Medicinal Chemistry, (24 Aug 2006) Vol. 49, No. 17, pp. 5363-5371. .
Refs: 44
ISSN: 0022-2623 CODEN: JMCMAR

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Sep 2006
Last Updated on STN: 14 Sep 2006

AB Pyrazolo[1',5':1,6]pyrimido[4,5-d]**pyridazin**-4(3H)-ones and their analogues, potentially useful for the treatment of erectile dysfunction, were synthesized and evaluated as **inhibitors** of phosphodiesterase 5 (PDE5). Several compounds showed IC(50) values in the low nanomolar range, and in particular, compound 5r, displaying high potency toward PDE5 (IC(50) = 8.3 nM) and high selectivity versus PDE6 (240-fold) appeared to be a very promising new lead both in comparison with the potent but not selective sildenafil and in comparison with

some analogues previously reported by us. SAR studies in this triheterocyclic scaffold led us to conclude that the best arranged groups are a methyl in position 1, a benzyl in position 3, a phenyl in position 9, and a linear four-carbon chain in position 6. .COPYRGT. 2006 American Chemical Society.

L43 ANSWER 29 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2

ACCESSION NUMBER: 2006312087 EMBASE Full-text
TITLE: Local anti-inflammatory effect and behavioral studies on new PDE4 **inhibitors.**
AUTHOR: Pieretti S.; Dominici L.; Di Giannuario A.; Cesari N.; **Dal Piaz V.**
CORPORATE SOURCE: S. Pieretti, Department of Drug Research and Evaluation, Italian National Institute of Health, Rome, Italy. pieretti@iss.it
SOURCE: Life Sciences, (17 Jul 2006) Vol. 79, No. 8, pp. 791-800. .
Refs: 45
ISSN: 0024-3205 CODEN: LIFSAK
PUBLISHER IDENT.: S 0024-3205(06)00188-3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Aug 2006
Last Updated on STN: 1 Aug 2006

AB Phosphodiesterase 4 (PDE4) **inhibitors** are effective anti-inflammatory drugs, although some adverse effects are observed in animals and humans. These effects have forced researchers to find new PDE4 **inhibitors** with less adverse effects. We recently reported the synthesis of novel heterocyclic-fused **pyridazinones** that inhibit PDE4. As a first step in the study of the anti-inflammatory properties of these compounds, we studied the effects of local administration of these **pyridazinone** derivatives in a mouse model of acute inflammation. We found that 6-Benzyl-3-methyl-4-phenylpyrazolo[3,4-d]**pyridazin**-7(6H)-one (CC4), ethyl 6,7-dihydro-6-ethyl-3-methyl-7-oxo-4-phenyl-thieno[2,3-d] **pyridazine**-2-carboxylate (CC6) and ethyl 6,7-dihydro-6-ethyl-3- methyl-4-phenyl-1H-pyrrolo[2,3-d]**pyridazine**-2-carboxylate (CC12) reduced the paw edema induced by zymosan in mice as rolipram (the PDE4 inhibitor prototype with anti-inflammatory activity) and indomethacin did. It is well known that rolipram locally administered induces some adverse effects such as hyperalgesia. Thus, we studied this effect after local administration of CC4, CC6 and CC12 in the formalin test. We found that CC6 induced hyperalgesic effects, whereas CC4 and CC12 did not change the nociceptive threshold. Furthermore, we found that rolipram and CC6 reduced locomotor activity, whereas CC4 and CC12 did not change locomotor performance of the mice. Since CC4 and CC12 neither affected the nociceptive threshold nor changed the locomotor performance of mice, they appear more suitable than CC6 for future studies on animals and could be developed as an anti-inflammatory drug for humans. .COPYRGT. 2006 Elsevier Inc. All rights reserved.

L43 ANSWER 30 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2005174396 EMBASE Full-text
TITLE: New pyrazolo[1',5':1,6]pyrimido[4,5-d]**pyridazin**

-4(3H)-ones as potent and selective PDE5 **inhibitors**.
AUTHOR: Feixas J.; **Giovannoni M.P.**; **Vergelli C.**; Gavalda A.; Cesari N.; Graziano A.; **Dal Piaz V.**
CORPORATE SOURCE: V. Dal Piaz, Dipto. di Scienze Farmaceutiche, Universita di Firenze, Via U. Schiff 6, Sesto Fiorentino 50019, Firenze, Italy. vittorio.dalpiaz@unifi.it
SOURCE: Bioorganic and Medicinal Chemistry Letters, (2 May 2005) Vol. 15, No. 9, pp. 2381-2384. .
Refs: 27
ISSN: 0960-894X CODEN: BMCLE8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 May 2005
Last Updated on STN: 26 May 2005
AB A series of potent PDE5 **inhibitors** with high selectivity versus PDE6 isoenzymes was identified. .COPYRGT. 2005 Elsevier Ltd. All rights reserved.

L43 ANSWER 31 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4
ACCESSION NUMBER: 2003113289 EMBASE Full-text
TITLE: Novel 3-arylamino- and 3-cycloalkylamino-5,6-diphenyl-**pyridazines** active as ACAT **inhibitors**
.
AUTHOR: Toma L.; **Giovannoni M.P.**; **Vergelli C.**; **Dal Piaz V.**; Kwon B.-M.; Kim Y.-K.; Gelain A.; Barlocco D.
CORPORATE SOURCE: L. Toma, Dipartimento di Chimica Organica, Universita di Pavia, Via Taramelli 10, 27100 Pavia, Italy. toma@chifis.unipv.it
SOURCE: Archiv der Pharmazie, (2002) Vol. 335, No. 11-12, pp. 563-566. .
Refs: 13
ISSN: 0365-6233 CODEN: ARPMAS
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Mar 2003
Last Updated on STN: 27 Mar 2003
AB A new series of **pyridazine** derivatives, structurally related to the previously reported ACAT **inhibitors** 3-(cyclo)alkylamino-5,6-diphenyl-**pyridazines**, were synthesized and tested for their inhibitory properties. Substitution of the 3-alkylamino chain with a phenylamino group maintains activity. In contrast, the presence of either substituents on the phenylamino group or aliphatic rings having more or less than six carbon atoms lowers it.

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ACCESSION NUMBER: 97142951 EMBASE Full-text
DOCUMENT NUMBER: 1997142951
TITLE: Novel heterocyclic-fused **pyridazinones** as potent and selective phosphodiesterase IV **inhibitors**.
AUTHOR: Piaz V.D.; **Giovannoni M.P.**; Castellana C.; Palacios J.M.; Beleta J.; Domenech T.; Segarra V.
CORPORATE SOURCE: V.D. Piaz, Dipto. di Scienze Farmaceutiche, via Gino Capponi 9, 50121 Firenze, Italy
SOURCE: Journal of Medicinal Chemistry, (1997) Vol. 40, No. 10, pp. 1417-1421. .
Refs: 31
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 1997
Last Updated on STN: 4 Jun 1997

AB A series of 6-aryl-4,5-heterocyclic-fused **pyridazinones** were designed and synthesized as selective phosphodiesterase (PDE) IV **inhibitors**. Biological evaluation of these compounds demonstrated a good selectivity profile toward the PDE IV family and greatly attenuated affinity for the Rolipram high-affinity binding site that seems to be responsible for undesiderable side effects. Structure-activity relationships (SARs) studies showed that the presence of an ethyl group at **pyridazine** N-2 is associated with the best potency and selectivity profile.

L43 ANSWER 33 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002129062 EMBASE Full-text
TITLE: Airway relaxant and anti-inflammatory properties of a PDE4 inhibitor with low affinity for the high-affinity rolipram binding site.
AUTHOR: Martin C.; Goggel R.; **Dal Piaz V.**; **Vergelli C.**; **Giovannoni M.P.**; Ernst M.; Uhlig S.
CORPORATE SOURCE: S. Uhlig, Division of Pulmonary Pharmacology, Research Centre Borstel, Parkallee 22, 23845 Borstel, Germany. suhlig@fzborstel.de
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (2002) Vol. 365, No. 4, pp. 284-289. .
Refs: 31
ISSN: 0028-1298 CODEN: NSAPCC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 18 Apr 2002
Last Updated on STN: 18 Apr 2002

AB **Inhibitors** of phosphodiesterase 4 (PDE4) possess bronchospasmolytic and anti-inflammatory properties, which make them very attractive drugs for the

treatment of asthma and COPD. Unfortunately, many PDE4 **inhibitors** also produce central nervous and gastrointestinal side effects, which have limited their clinical application. PDE4 has two binding sites for the archetypal PDE4 inhibitor rolipram, and it has been suggested that binding to the high-affinity rolipram binding site (HARBS) is responsible for the side effects of PDE4 **inhibitors**. Recently, we have synthesised the PDE4 inhibitor CC3 which shows low affinity to the HARBS. In the present study we investigated the bronchospasmolytic and anti-inflammatory properties of this novel compound in comparison to rolipram and the PDE3 inhibitor motapizone. The airway-relaxant properties of the PDE **inhibitors** were analysed in rat precision-cut lung slices (PCLS) in which airways were contracted by methacholine or in passively sensi-tised PCLS exposed to ovalbumin. The anti-inflammatory properties were investigated by measuring the release of TNF from endotoxin-treated human monocytes. Up to concentrations of 10μM none of the PDE **inhibitors** significantly affected bronchoconstriction elicited by 10μM methacholine. However, if rolipram or CC3 were given in combination with motapizone, methacholine-induced bronchoconstriction was concentration-dependently attenuated. Allergen-induced bronchoconstriction in passively sensitised PCLS was attenuated by CC3 (IC(50) 2.7 μM), rolipram (0.23μM) and motapizone (8μM). Combination of equimolar concentrations of motapizone and CC3 (0.34μM) or rolipram (0.005μM) showed an additive effect. Endotoxin-induced TNF release from human monocytes was attenuated by all three PDE **inhibitors**, i.e. CC3 (IC(50) 4.6 μM), rolipram (0.18 μM) and motapizone (5.8μM). Our findings suggest that PDE4 **inhibitors** with only low affinity for the HABRS have bronchospas-molytic and anti-inflammatory properties.

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ACCESSION NUMBER: 97024236 EMBASE Full-text
DOCUMENT NUMBER: 1997024236
TITLE: Synthesis and evaluation as PDE IV **inhibitors** of 4,5-hetero-condensed-6-phenyl-3(2H)-**pyridazinones**.
AUTHOR: **Dal Piaz V.**; **Giovannoni M.P.**; Castellana C.; Palacios J.M.; Beleta J.; Domenech T.; Segarra V.
CORPORATE SOURCE: V. Dal Piaz, Dipto. di Scienze Farmaceutiche, Via Gino Capponi 9, 50121 Firenze, Italy
SOURCE: Acta Pharmaceutica Hungarica, (1996) Vol. 66, No. SUPPL., pp. S33-S34. .
Refs: 9
ISSN: 0001-6659 CODEN: APHGAO
COUNTRY: Hungary
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 1997
Last Updated on STN: 14 Feb 1997

L43 ANSWER 35 OF 38 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:412197 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200412197
TITLE: 1,2,4-triazolo(4,3-b)pyrido(3,2-d)**pyridazine** derivatives and pharmaceutical compositions containing them.
AUTHOR(S): **Gracia Ferrer, Jordi** [Inventor, Reprint author]; Crespo Crespo, Ma Isabel [Inventor]; Vega

Noverola, Armando [Inventor]; Fernandez Garcia, Andres [Inventor]
CORPORATE SOURCE: Barcelona, Spain
ASSIGNEE: Almirall Prodesfarma, S.A., Barcelona, Spain
PATENT INFORMATION: US 6407108 20020618
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 18, 2002) Vol. 1259, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Jul 2002
Last Updated on STN: 31 Jul 2002

AB Heterocyclic compounds of formula(I), ##STR1## wherein R1 represents a hydrogen atom or a --(CH2)m --Y group, wherein m is an integer from 0 to 4 and Y represents an alkyl, haloalkyl, alkoxy, alkoxycarbonyl, C3 -C7 cycloalkyl, norbornyl or phenylalkenyl group, or an aromatic group which aromatic group may optionally be substituted by one or more halogen atoms; R2 represents an aromatic group which aromatic group may optionally be substituted by one or more halogen atoms or alkyl, alkoxy, C3 -C6 cycloalkoxy, methylenedioxy, nitro, dialkylamino or trifluoromethyl groups, and R3 represents a hydrogen or halogen atom or an alkyl group, and pharmaceutically acceptable salts thereof, processes for preparing the same are disclosed herein. The compounds are phosphodiesterase 4 **inhibitors**.

L43 ANSWER 36 OF 38 MEDLINE on STN
ACCESSION NUMBER: 2001676035 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11708931
TITLE: 5,6-Diphenylpyridazine derivatives as acyl-CoA:cholesterol acyltransferase **inhibitors** .
AUTHOR: **Giovannoni M P**; Piaz V D; Kwon B M; Kim M K; Kim Y K; Toma L; Barlocco D; Bernini F; Canavesi M
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, via G. Capponi 9, 50121 Firenze, Italy.. mariapaola.giovannoni@unifi.it
SOURCE: Journal of medicinal chemistry, (2001 Nov 22) Vol. 44, No. 24, pp. 4292-5.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 28 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 12 Dec 2001

AB Alkyl-5,6-diphenylpyridazine derivatives combining several main features of ACAT **inhibitors**, such as a long alkyl side chain linked to a heterocycle and the o-diphenyl system, were synthesized and tested. Moreover, modeling studies on representative terms were performed. Some compounds displayed ACAT inhibition in the micromolar range, both on the enzyme isolated from rat liver microsomes and in cell-free homogenate of murine macrophages.

L43 ANSWER 37 OF 38 MEDLINE on STN
ACCESSION NUMBER: 1998032732 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9366028

TITLE: Chiral resolution and absolute configuration of the enantiomers of 5-acetyl-2-methyl-4-methylsulfinyl-6-phenyl-3(2H)-**pyridazinone** and evaluation of their platelet aggregation inhibitory activity.
AUTHOR: Azzolina O; **Dal Piaz V**; Collina S; **Giovannoni M P**; Tadini C
CORPORATE SOURCE: Dipartimento di Chimica Farmaceutica, Universita di Pavia, Italy.
SOURCE: Chirality, (1997) Vol. 9, No. 7, pp. 681-5.
Journal code: 8914261. ISSN: 0899-0042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 29 Jan 1998
Last Updated on STN: 29 Jan 1998
Entered Medline: 12 Jan 1998

AB In a series of 5-acyl-6-phenyl-2,4-substituted-3(2H)-pyridaziones the derivative 1a, with a sulfur stereogenic center, had the most potent activity as human platelet aggregation inhibitor. The resolution of rac-1a was successfully performed by chiral chromatography on Chiralcel OD-R, OD-H, and Chiralpak AD columns and scaled up to a preparative level. The absolute configuration of (-)-(S)-1a was determined by X-ray crystallographic analysis. In vitro human platelet aggregation inhibitory activity was evaluated. Both the enantiomers showed IC50 values in the same micromolar range, but the (-)-(S) isomer was slightly more potent [(S)/(R) potency ratio was 4/1].

L43 ANSWER 38 OF 38 MEDLINE on STN
ACCESSION NUMBER: 97453368 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9299216
TITLE: Study of the antisecretory and antiulcer mechanisms of a new indenopirydazinone derivative in rats.
AUTHOR: Barocelli E; Chiavarini M; Ballabeni V; Barlocco D; Vianello P; **Dal Piaz V**; Impicciatore M
CORPORATE SOURCE: Istituto di Farmacologia e Farmacognosia, Universita degli Studi di Parma, Italy.
SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (1997 May) Vol. 35, No. 5, pp. 487-92.
Journal code: 8907422. ISSN: 1043-6618.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 24 Dec 1997
Entered Medline: 24 Nov 1997

AB The present study investigates the antisecretory and antiulcer mechanisms of a new indenopyridazinone derivative previously reported to inhibit gastric acid secretion in pylorus-ligated rats and to prevent gastric ulcerations induced by indomethacin or ethanol in the same animal species. The new compound was tested on the acid hypersecretion induced by histamine, pentagastrin and bethanechol in in vivo and in vitro experimental models. Furthermore, its influence on the mucosal layer adhering the gastric wall in indomethacin-treated rats was considered. Ranitidine was selected as a reference drug. The results obtained demonstrated that the new molecule, at variance with ranitidine, exerts antiulcer activity mainly enhancing the gastric mucosal

integrity and simultaneously inhibiting the gastric acid hypersecretion evoked exclusively by cholinergic pulses. Therefore, an involvement of a neuronal rather than an effectorial mechanism has been suggested. Due to these mechanisms of action it clearly differentiates from ranitidine and its possible application in the peptic disease resistant to H2-blockers could be speculated.

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=> d his nofile

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     FILE 'HCAPLUS' ENTERED AT 10:34:12 ON 15 DEC 2006
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                 SEL RN

     FILE 'REGISTRY' ENTERED AT 10:34:38 ON 15 DEC 2006
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L3               STR
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L15          23 SEA ABB=ON  PLU=ON  L14 AND (THU OR BIOL OR BSU)/RL
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L17          34 SEA ABB=ON  PLU=ON  L15 OR L16
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L18          77 SEA ABB=ON  PLU=ON  DAL PIAZ, V?/AU
L19           4 SEA ABB=ON  PLU=ON  AGUILAR IZQUIERDO, N?/AU
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L23          41 SEA ABB=ON  PLU=ON  GIOVANNONI, M?/AU
L24          15 SEA ABB=ON  PLU=ON  VERGELLI, C?/AU
L25          27 SEA ABB=ON  PLU=ON  L14 AND ((L18 OR L19 OR L20 OR L21 OR
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L26           5 SEA ABB=ON  PLU=ON  L16 NOT L25
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L27           6 SEA SSS SAM L9
L28         102 SEA SSS FUL L9

     FILE 'REGISTRY' ENTERED AT 10:53:59 ON 15 DEC 2006
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L30           0 SEA ABB=ON  PLU=ON  L11 AND BIOSIS/LC
L31           0 SEA ABB=ON  PLU=ON  L11 AND EMBASE/LC

     FILE 'EMBASE, BIOSIS, MEDLINE' ENTERED AT 10:54:47 ON 15 DEC 2006
L32           0 SEA ABB=ON  PLU=ON  AGUILAR IZQUIERDO, N?/AU
L33           2 SEA ABB=ON  PLU=ON  BUIL ALBERO MARIA, A?/AU
L34           0 SEA ABB=ON  PLU=ON  CARRASCAL RIERA, M?/AU
L35           2 SEA ABB=ON  PLU=ON  GRACIA FERRER, J?/AU
L36         113 SEA ABB=ON  PLU=ON  GIOVANNONI, M?/AU
L37          26 SEA ABB=ON  PLU=ON  VERGELLI, C?/AU
L38          35 SEA ABB=ON  PLU=ON  (L32 OR L33 OR L34 OR L35 OR L36 OR
                L37) AND (PYRIDAZIN? AND INHIBITORS?)
                D IBIB
L39         117 SEA ABB=ON  PLU=ON  DAL PIAZ, V?/AU
L40          35 SEA ABB=ON  PLU=ON  L39 AND (PYRIDAZIN? AND INHIBITORS?)
L41          39 SEA ABB=ON  PLU=ON  L38 OR L40

     FILE 'HCAPLUS' ENTERED AT 11:16:50 ON 15 DEC 2006
                D L26 4-5 IBIB FHITSTR
                SEL L26 HIT RN 1-
                D QUE L16
L42           5 SEA ABB=ON  PLU=ON  L16 NOT L25
                D L42 1-5 IBIB ED AB HITSTR HITIND
                D QUE L25
                E QUE L34
                D QUE L41

     FILE 'HCAPLUS, EMBASE, BIOSIS, MEDLINE' ENTERED AT 11:19:51 ON 15 DEC
     2006
L43          38 DUP REM L25 L41 (28 DUPLICATES REMOVED)
                     ANSWERS '1-27' FROM FILE HCAPLUS
                     ANSWERS '28-34' FROM FILE EMBASE
                     ANSWER '35' FROM FILE BIOSIS
                     ANSWERS '36-38' FROM FILE MEDLINE
                D L43 1-38 IBIB AB
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